REMARKS

Claims 1, 2 and 6-20 are currently pending. Claims 3-5 were previously canceled.

Claims 11, 12, 15 and 16 have been withdrawn.

Claims 1 and 2 have been amended to remove sequences not elected and the proviso.

Claims 1, 2, 6-10, 13, 14 and 17-20 have been amended to correct antecedent basis as discussed below.

No new matter has been entered.

Drawings

The Examiner requires new corrected drawings alleging that the drawings submitted are informal drawings not acceptable for publication. Applicants traverse.

Replacement drawings were filed with the United States Patent and Trademark Office on March 3, 2009, a copy of the E-Filing Receipt is attached. Applicants submit that the formal drawings produced by a competent patent draftsperson and submitted on March 3, 2009, which are accessible on PAIR, are perfectly legible, including Figure 5. Therefore the objection to the drawings should be dismissed. In the event that the Examiner has some further reason for objection to the drawings, Applicants hereby request more specific information that will enable them to rectify the drawings appropriately.

Objections

The Examiner has objected to the Specification, stating that SEQ ID NO. identifiers are missing for sequences on pages 895, 896, 900, 901 and 909.

Applicants have amended the Specification to include the SEQ ID NOs for the sequences present on these pages. These sequences and the corresponding SEQ ID NOs appear in the Sequence Listing that was filed on April 18, 2005.

Rejections Under 35 USC § 112, 2nd Paragraph

The Examiner rejects claims 1 and 2, alleging that it is unclear whether the recitations in parentheses are intended to be claim limitations. Applicants have deleted this portion of the claim, thereby overcoming the rejection.

The Examiner rejects claim 1(b) stating that a complementary sequence reads on a 2-mer and suggests entering "fully" in front of "complementary." Applicants have so amended the claim, thereby overcoming the rejection.

The Examiner rejects claim 1(c), stating that this subsection reads on a 2-mer and contends that the term "about" is unclear. The Examiner suggests reciting a function for the hybridizing sequence and deleting the term "about." Applicants have so amended the claims, thereby overcoming the rejections. Furthermore, in support of the function recited Applicants also provide the annotations associated with the claimed sequence which were presented in priority applications 09/513,996 (filed February 25, 2000) and 10/621,442 (filed July 18, 2003), both of which were incorporated by reference in their entirety.

The Examiner has rejected claim 2(a), stating that "a fragment thereof" reads of a single base and suggests reciting a function for the fragment. Applicants have so amended the claim, thereby overcoming the rejection.

The Examiner has rejected claim 2(b), stating that "a complement" reads on a 2-mer and suggests inserting "full-length" prior to "complement." The Examiner also rejects the use of the phrase "a fragment thereof" and suggests reciting a function for the fragment. Applicants have so amended the claim, thereby overcoming the rejection.

The Examiner suggests replacing the article "an" in claim 9 with "the." Applicants have so amended the claim, thereby overcoming the rejection.

The Examiner suggests replacing the article "a" in claims 10, 14 and 18 with "the." Applicants have so amended the claims, thereby overcoming the rejection.

The Examiner suggests replacing the article "a" in claim 17 with "the." Applicants have so amended the claim, thereby overcoming the rejection.

The Examiner suggests replacing the article "a" in claims 19 and 20 with "the." Applicants have so amended the claims, thereby overcoming the rejection.

Rejections Under 35 USC § 101

The Examiner has rejected claims 1, 2, 6-10, 13, 14 and 17-20 for lack of utility. The Examiner contends that the Specification does not provide a function or utility for SEQ ID NO:16117 (encoding SEQ ID NO:16118), and the skilled artisan would not understand how the sequence could be used. The Examiner further alleges that the claimed invention does not have a specific and substantial utility and neither does it have a well-established utility. Applicants respectfully traverse.

Applicants provide, in support of the function recited, the annotations associated with the claimed sequence which were presented in priority applications 09/513,996 (filed February 25, 2000) and 10/621,442 (filed July 18, 2003), both of which were incorporated in their entirety. As can be seen from these annotations, the claimed sequence was identified as having similarity to a cyclin and residues 5 to 124 of SEQ ID NO:16118 are a cyclin_N domain. Applicants submit that cyclins have a well-established utility that is well known and understood by those of skill in the art practicing in this field. Therefore, Applicants have fulfilled the requirement for utility and request removal of the rejection.

The Examiner also notes that these claims are similarly rejected under 35 USC § 112, first paragraph. Applicants submit that the attached information and statements above equally fulfill the requirement for utility under 35 USC § 112, first paragraph and request removal of this rejection.

Rejections Under 35 USC § 112, 1st Paragraph

The Examiner has rejected claims under 35 USC § 112, first paragraph for lack of enablement. The Examiner contends that, in addition to lacking utility, the recitation of 85-95% sequence identity, complementary sequence and sequence which hybridize at 5-10°C below the melting temperature, as well as fragments of the elected sequence. Applicants respectfully traverse.

Applicants have amended the claims as discussed above, which Applicants submit overcome the rejections based on complementary sequences and hybridizing sequences.

Applicants have also amended the claims to recite at least 95% identity. Here, Applicants point out that the degeneracy of the genetic code alone provides nucleic acid sequences which would encode SEQ ID NO:16118 and have 95% identity to SEQ ID NO:16117. Hence this aspect of the claims is certainly enabled. With respect to where the skilled artisan might make changes to the amino acid sequence, Applicants note that cyclins generally contain at least one cyclin domain, such as a cyclin box, an N-terminus cyclin domain and/or a C-terminus cyclin domain (see attached Pfam statement). For example, in SEQ ID NO:16118 the cyclin_N domain is at residues 5 to 124. The skilled artisan would understand that amino acid substitutions would not be made in these conserved regions or in any other known domains that were identified in the sequence. Consequently, in view of all of these considerations, Applicants request removal of the rejection.

Rejections Under 35 USC § 102

The Examiner has rejected claims 1, 2, 6, 8-10, 13 and 14 as anticipated by Lin *et al.* under 35 USC § 102(b). The Examiner alleges that Lin *et al.* teach a nucleic acid sequence encoding an amino acid sequence having 100% sequence identity to SEQ ID NO:16118. Applicants respectfully traverse.

The sequence denoted as SEQ ID NO:16118 in the current application is also present in the US Serial Number 60/128,234 as SEQ ID NO:10 at page 1006 of the Table submitted with the application, a copy of which is attached hereto. Applicants also include a list of the priority sequences identical to SEQ ID NO:16118 and an alignment of them. The instant application claims priority to US Serial Number 60/128,234, which was filed on April 6, 1999. Because Lin *et al.* published December 16, 1999, the priority claim of the instant application pre-dates the Lin *et al.* publication. Therefore Lin *et al.* cannot support an anticipation rejection and Applicants request removal of the rejection.

The Examiner rejects claims 1, 2, 6-10, 13, 14 and 17-20 under 35 USC § 102(b) as anticipated by Alexandrov *et al.*, published September 6, 2000. Applicants respectfully traverse.

The sequence denoted as SEQ ID NO:16118 in the current application is also present in the US Serial Number 09/513,996, which is the US equivalent of the European Application published as EP1033405 and which was filed in the United State Patent and Trademark Office

on February 25, 2000 (see attached priority sequence list and alignment). The instant application claims priority to US Serial Number 09/513,996. Therefore, because Alexandrov *et al.* published September 6, 2000 and the priority claim of the instant application pre-dates the Alexandrov *et al.* publication, the Alexandrov *et al.* cannot support an anticipation rejection. Applicants therefore request removal of the rejection.

Conclusion

In view of the above remarks, all of the claims are submitted as defining non-obvious, patentable subject matter. Reconsideration of the rejections and allowance of the claims are respectfully requested. Applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Susan W. Gorman, Ph.D., Reg. No. 47,604 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee of $1,110.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: May 12, 2011

Respectfully submitted,

#47,604

By _____
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Enclosures: March 3, 2009 E-Filing Receipt for formal drawings submitted
Excerpt from Table I of US Serial Number 09/513,996 (filed February 25, 2000)
Except from Table 1-02 of US Serial Number 10/621,442 (filed July 18, 2003)
List of priority sequences and alignment of priority sequences
Pfam Family Cyclin_N

Electronic Acknowledgement Receipt

EFS ID:	4892501
Application Number:	10645822
International Application Number:	
Confirmation Number:	7309
Title of Invention:	Sequence-determined DNA fragments and corresponding polypeptides encoded therapy
First Named Inventor/Applicant Name:	Nickolai Alexandrov
Customer Number:	02292
Filer:	Susan W. Gorman./Alison Lalonde
Filer Authorized By:	Susan W. Gorman.
Attorney Docket Number:	2750-1571P
Receipt Date:	03-MAR-2009
Filing Date:	22-AUG-2003
Time Stamp:	13:14:38
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Applicant Response to Pre-Exam Formalities Notice	20090303ReplyToNTCAP.pdf	131334 2c9eeba537e91f2a12e932cabce1ac7641083 38e	no	2

Warnings:	
Information:	

2	Drawings-only black and white line drawings	20090303Fig1.pdf	166422 12e2efee338e0f96fd92eed845334ad8067f5fa4	no	1
Warnings:					
Information:					
3	Drawings-only black and white line drawings	20090303Fig2.pdf	106448 a1d6b5ab4ff162cfc53aa493ac793b25b1fca662	no	1
Warnings:					
Information:					
4	Drawings-only black and white line drawings	20090303Fig3.pdf	86143 24ae4525123ccf9afbb8b74941f36a08e651eb19	no	1
Warnings:					
Information:					
5	Drawings-only black and white line drawings	20090303Fig4.pdf	34785 5a92dd09a60e4d257be68d3ef8c81575a900f3e3	no	1
Warnings:					
Information:					
6	Drawings-only black and white line drawings	20090303Fig5.pdf	46501 ec93d1b7b622ca515f00986533cb1dc79ce5a574	no	1
Warnings:					
Information:					
7	Drawings-only black and white line drawings	20090303Fig6.pdf	52520 88752398bd9286a0c728d5a694b4b2a5fea0d977	no	1
Warnings:					
Information:					
8	Drawings-only black and white line drawings	20090303Fig7.pdf	68070 33b65e8e4f6f792641a19f144a559ec033dc6bbb	no	1
Warnings:					
Information:					
		Total Files Size (in bytes):	692223		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

SEQ ID NO. 16180 from US Serial No. 09/513,966

```
2750-0709  09/513,996  25-Feb-00

From TABLE 1

Max Len. Seq. :
rel to:
Clone IDs:
      22595
(Ac) cDNA SEQ
      - Pat. Appln. SEQ ID NO: 16179
      - Ceres SEQ ID NO: 1388814
      - SEQ 16179 w. TSS:
        5

   PolyP SEQ
       - Pat. Appln. SEQ ID NO 16180
       - Ceres SEQ ID NO 1388815
       - Loc. SEQ ID NO 16179: @ 119 nt.

       (C) Pred. PP Nom. & Annot.
       (Dp) Rel. AA SEQ
           - Align. NO 11180
           - gi No 2739368
           - Desp. :
           - % Idnt. : 100
           - Align. Len.: 361
           - Loc. SEQ ID NO 16180: 56 -> 416 aa.
```

Note: the GI number noted in the above table was annotated in NCBI as a 'putative cyclin' as of January 2, 1998.

SEQ ID NO. 9497 from US Serial No. 10/621,442

2750-1568US 10/621,442 July 18, 2003

Note: we claim priority and incorporate by docket number only since we did not have the application serial number when we filed 2750-1571.

From TABLE 1-02

(Ac) cDNA SEQ

- Pat. Appln. SEQ ID NO: 9496
- Ceres SEQ ID NO: 2994737

PolyP SEQ

- Pat. Appln. SEQ ID NO 9497
- Ceres SEQ ID NO 2994738
- Loc. SEQ ID NO 9496: @ 117 nt.

(C) Pred. PP Nom. & Annot.

(Dp) Rel. AA SEQ

- Align. NO 48437
- gi No 7290261
- Desp. : (AE003423) CG16903 gene product [Drosophila melanogaster]
- % Idnt. : 37.7
- Align. Len.: 429

- Loc. SEQ ID NO 9497: 1 -> 412 aa.

- Align. NO 48438

- gi No 7670474

- Desp. : (AB041605) unnamed protein product [Mus musculus]

- % Idnt. : 38.5

- Align. Len.: 394

- Loc. SEQ ID NO 9497: 1 -> 381 aa.

- Align. NO 48439

- gi No 6691833

- Desp. : (AL034388) /prediction=(method:""genscan"", version:""1.0"")~/match=(desc:""CYCLIN T2B"", species:""Homo sapiens (Human)"", ranges:(query:1107..1382, target:SPTREMBL::O60583:108..17, score:""131.00""),

- % Idnt. : 37.3

- Align. Len.: 417

- Loc. SEQ ID NO 9497: 1 -> 400 aa.

- Align. NO 48440

- gi No 5823554

- Desp. : (AF180920) cyclin L ania-6a [Homo sapiens]

- % Idnt. : 35.5

- Align. Len.: 426

- Loc. SEQ ID NO 9497: 1 -> 415 aa.

- Align. NO 48441

- gi No 5579444

- Desp. : (AF030091) cyclin ania-6a [Rattus norvegicus]

- % Idnt. : 35.2

- Align. Len.: 426

- Loc. SEQ ID NO 9497: 1 -> 415 aa.

- Align. NO 48442

- gi No 5453421

- Desp. : (AF159159) cyclin ania-6a [Mus musculus]

- % Idnt. : 35.2

- Align. Len.: 426

- Loc. SEQ ID NO 9497: 1 -> 415 aa.

- Align. NO 48443

- gi No 6665778

- Desp. : (AF211859) cyclin ania-6b [Mus musculus]

- % Idnt. : 48.3

- Align. Len.: 182

- Loc. SEQ ID NO 9497: 1 -> 176 aa.

- Align. NO 48444

- gi No 4502625

- Desp. : ref|NP_003849.1| cyclin K >gi|3746549|gb|AAD09978.1| (AF060515) cyclin K [Homo sapiens]

- % Idnt. : 33.2

- Align. Len.: 251

- Loc. SEQ ID NO 9497: 9 -> 246 aa.

- Align. NO 48445

- gi No 4502629

- Desp. : ref|NP_001232.1| cyclin T2 >gi|2981198|gb|AAC39665.1| (AF048731) cyclin T2a [Homo sapiens]

- % Idnt. : 31.1

- Align. Len.: 223

- Loc. SEQ ID NO 9497: 5 -> 223 aa.

- Align. NO 48446

- gi No 4502629

- Desp. : ref|NP_001232.1| cyclin T2 >gi|2981198|gb|AAC39665.1| (AF048731) cyclin T2a [Homo sapiens]

- % Idnt. : 25.2

- Align. Len.: 119

- Loc. SEQ ID NO 9497: 305 -> 416 aa.

List of Priority Sequences Identical to SEQ ID NO. 16118

sequences 2750-1571

>SEQ_ID_NO_16180 2750-0709
MIYTAIDNFYLSDEQLKASPSRKDGIDETTEISLRIYGCDLIQEGGILLKLPQAVMATGQ
VLFQRFYCKKSLAKFDVKIVAASCVWLASKLEENPKKARQVIIVFHRMECRRENLPLEHL
DMYAKKFSELKVELSRTERHILKEMGFVCHVEHPHKFISNYLATLETPPELRQEAWNLAN
DSLRTTLCVRFRSEVVACGVVYAAARRFQVPLPENPPWWKAFDADKSSIDEVCRVLAHLY
SLPKAQYISVCKDGKPFTFSSRSGNSQGQSATKDLLPGAGEAVDTKCTAGSANNDLKDGM
VTTPHEKATDSKKSGTESNSQPIVGDSSYERSKVGDRERESDREKERGRERDRGRSHRGR
DSDRDSDRERDKLKDRSHHRSRDRLKDSGGHSDKSRHHSSRDRDYRDSSKDRRRHH

>SEQ_ID_NO_10 from table 2750-0416 page 1006
MIYTAIDNFYLSDEQLKASPSRKDGIDETTEISLRIYGCDLIQEGGILLKLPQAVMATGQ
VLFQRFYCKKSLAKFDVKIVAASCVWLASKLEENPKKARQVIIVFHRMECRRENLPLEHL
DMYAKKFSELKVELSRTERHILKEMGFVCHVEHPHKFISNYLATLETPPELRQEAWNLAN
DSLRTTLCVRFRSEVVACGVVYAAARRFQVPLPENPPWWKAFDADKSSIDEVCRVLAHLY
SLPKAQYISVCKDGKPFTFSSRSGNSQGQSATKDLLPGAGEAVDTKCTAGSANNDLKDGM
VTTPHEKATDSKKSGTESNSQPIVGDSSYERSKVGDRERESDREKERGRERDRGRSHRGR
DSDRDSDRERDKLKDRSHHRSRDRLKDSGGHSDKSRHHSSRDRDYRDSSKDRRRHH

>SEQ_ID_NO_9497 2750-1568US
MIYTAIDNFYLSDEQLKASPSRKDGIDETTEISLRIYGCDLIQEGGILLKLPQAVMATGQ
VLFQRFYCKKSLAKFDVKIVAASCVWLASKLEENPKKARQVIIVFHRMECRRENLPLEHL
DMYAKKFSELKVELSRTERHILKEMGFVCHVEHPHKFISNYLATLETPPELRQEAWNLAN
DSLRTTLCVRFRSEVVACGVVYAAARRFQVPLPENPPWWKAFDADKSSIDEVCRVLAHLY
SLPKAQYISVCKDGKPFTFSSRSGNSQGQSATKDLLPGAGEAVDTKCTAGSANNDLKDGM
VTTPHEKATDSKKSGTESNSQPIVGDSSYERSKVGDRERESDREKERGRERDRGRSHRGR
DSDRDSDRERDKLKDRSHHRSRDRLKDSGGHSDKSRHHSSRDRDYRDSSKDRRRHH

>SEQ_ID_NO_16118 2750-1571P
MIYTAIDNFYLSDEQLKASPSRKDGIDETTEISLRIYGCDLIQEGGILLKLPQAVMATGQ
VLFQRFYCKKSLAKFDVKIVAASCVWLASKLEENPKKARQVIIVFHRMECRRENLPLEHL
DMYAKKFSELKVELSRTERHILKEMGFVCHVEHPHKFISNYLATLETPPELRQEAWNLAN
DSLRTTLCVRFRSEVVACGVVYAAARRFQVPLPENPPWWKAFDADKSSIDEVCRVLAHLY
SLPKAQYISVCKDGKPFTFSSRSGNSQGQSATKDLLPGAGEAVDTKCTAGSANNDLKDGM
VTTPHEKATDSKKSGTESNSQPIVGDSSYERSKVGDRERESDREKERGRERDRGRSHRGR
DSDRDSDRERDKLKDRSHHRSRDRLKDSGGHSDKSRHHSSRDRDYRDSSKDRRRHH

Alignment of Priority Sequences and SEQ ID NO. 16118

```
CLUSTALW format, MUSCLE (3.52) multiple sequence alignment


SEQ_ID_NO_16180      MIYTAIDNFYLSDEQLKASPSRKDGIDETTEISLRIYGCDLIQEGGILLKLPQAVNATGQ
SEQ_ID_NO_10         MIYTAIDNFYLSDEQLKASPSRKDGIDETTEISLRIYGCDLIQEGGILLKLPQAVNATGQ
SEQ_ID_NO_9497       MIYTAIDNFYLSDEQLKASPSRKDGIDETTEISLRIYGCDLIQEGGILLKLPQAVNATGQ
SEQ_ID_NO_16118      MIYTAIDNFYLSDEQLKASPSRKDGIDETTEISLRIYGCDLIQEGGILLKLPQAVNATGQ
                     ************************************************************

SEQ_ID_NO_16180      VLFQRFYCKKSLAKFDVKIVAA3CVWLASKLEENPKKARQVIIVFHRMECRRENLPLEHL
SEQ_ID_NO_10         VLFQRFYCKKSLAKFDVKIVAASCVWLASKLEENPKKARQVIIVFHRMECRRENLPLEHL
SEQ_ID_NO_9497       VLFQRFYCKKSLAKFDVKIVAASCVWLASKLEENPKKARQVIIVFHRMECRRENLPLEHL
SEQ_ID_NO_16118      VLFQRFYCKKSLAKFDVKIVAASCVWLASKLEENPKKARQVITVFHRMECRRENLPLEHL
                     ************************************************************

SEQ_ID_NO_16180      DMYAKKFSELKVELSRTERHILKEMGFVCHVEHPHKFISNYLATLETPPELRQEAWNLAN
SEQ_ID_NO_10         DMYAKKFSELKVELSRTERHILKEMGFVCHVEHPHKFISNYLATLETPPELRQEAWNLAN
SEQ_ID_NO_9497       DMYAKKFSELKVELSRTERHILKEMGFVCHVEHPHKFISNYLATLETPPELRQEAWNLAN
SEQ_ID_NO_16118      DMYAKKFSELKVELSRTERHILKEMGFVCHVEHPHKFISNYLATLETPPELRQEAWNLAN
                     ************************************************************

SEQ_ID_NO_16180      DSLRTTLCVRFRSEVVACGVVYAAARRFQVPLPENPPWWKAFDADKSSIDEVCRVLAHLY
SEQ_ID_NO_10         DSLRTTLCVRFRSEVVACGVVYAAARRFQVPLPENPPWWKAFDADKSSIDEVCRVLAHLY
SEQ_ID_NO_9497       DSLRTTLCVRFRSEVVACGVVYAAARRFQVPLPENPPWWKAFDADKSSIDEVCRVLAHLY
SEQ_ID_NO_16118      DSLRTTLCVRFRSEVVACGVVYAAARRFQVPLPENPPWWKAFDADKSSIDEVCRVLAHLY
                     ************************************************************

SEQ_ID_NO_16180      SLPKAQYISVCKDGKPFTFSSRSGNSQCQSATKDLLPGAGEAVDTKCTAGSANNDLKDGM
SEQ_ID_NO_10         SLPKAQYISVCKDGKPFTFSSRSGNSQCQSATKDLLPGAGEAVDTKCTAGSANNDLKDGM
SEQ_ID_NO_9497       SLPKAQYISVCKDGKPFTFSSRSGNSQCQSATKDLLPGAGEAVDTKCTAGSANNDLKDGM
SEQ_ID_NO_16118      SLPKAQYISVCKDGKPFTFSSRSGNSQCQSATKDLLPGAGEAVDTKCTAGSANNDLKDGM
                     ************************************************************

SEQ_ID_NO_16180      VTTPHEKATDSKKSGTESNSQPIVGDSSYERSKVGDRERESDREKERGRERDRGRSHRGR
SEQ_ID_NO_10         VTTPHEKATDSKKSGTESNSQPIVGDSSYERSKVGDRERESDREKERGRERDRGRSHRGR
SEQ_ID_NO_9497       VTTPHEKATDSKKSGTESNSQPIVGDSSYERSKVGDRERESDREKERGRERDRGRSHRGR
SEQ_ID_NO_16118      VTTPHEKATDSKKSGTESNSQPIVGDSSYERSKVGDRERESDREKERGRERDRGRSHRGR
                     ************************************************************

SEQ_ID_NO_16180      DSDRDSDRERDKLKDRSHHRSRDRLKDSGGHSDKSRHHSSRDRDYRDSSKDRRRHH
SEQ_ID_NO_10         DSDRDSDRERDKLKDRSHHRSRDRLKDSGGHSDKSRHHSSRDRDYRDSSKDRRRHH
SEQ_ID_NO_9497       DSDRDSDRERDKLKDRSHHRSRDRLKDSGGHSDKSRHHSSRDRDYRDSSKDRRRHH
SEQ_ID_NO_16118      DSDRDSDRERDKLKDRSHHRSRDRLKDSGGHSDKSRHHSSRDRDYRDSSKDRRRHH
                     ************************************************************


Global percentage of identity
  with gaps: 100.0%, without gaps: 100.0%


Percentage of identity based on short or long sequence
  short sequence: 100.0%, long sequence: 100.0%
```

Family: *Cyclin_N* (PF00134)

47 architectures 3041 sequences 12 interactions 373 species 158 structures

Summary
Domain organisation
Clans
Alignments
HMM logo
Trees
Curation & models
Species
Interactions
Structures

Jump to...
enter ID/acc

Summary

Pfam includes annotations and additional family information from a range of different sources. These sources can be accessed via the tabs below.

Wikipedia: Cyclin Pfam Interpro

The Pfam group coordinates the annotation of Pfam families in Wikipedia . This family is described by a Wikipedia entry entitled "Cyclin ". More...

Cyclin (Wikipedia Article)

Cyclins are a family of proteins that control the progression of cells through the cell cycle by activating cyclin-dependent kinase (Cdk) enzymes.[1]

Contents[show]

1 Function
2 Domain structure
3 Types
3.1 Main groups
3.2 Subtypes
3.3 Other proteins containing this domain
4 History
5 References
6 Further reading

Function

Expression of human cyclins through the cell cycle.

Cyclins are so named because their concentration varies in a cyclical fashion during the cell cycle. The oscillations of the cyclins, namely fluctuations in cyclin gene expression and destruction by proteolysis, induce oscillations in Cdk activity to drive the cell cycle. A cyclin forms a complex with Cdk, which begins to activate the Cdk, but the complete activation requires phosphorylation, as well. Complex formation results in activation of the Cdk active site. When concentrations in the cell are low, cyclins dissociate from Cdk, thus inhibiting enzymatic activity; this probably occurs due to a protein chain of the Cdk blocking the active site upon cyclin dissociation.[2][3] Cyclins themselves have no enzymatic activity. [citation needed]

They were discovered by R. Timothy Hunt in 1982 while studying the cell cycle of sea urchins.[4]

Cyclins, when bound with the dependent kinases, such as the p34 (cdc2) or cdk1 proteins, form the maturation-promoting factor. MPFs activate other proteins through phosphorylation. These phosphorylated proteins, in turn, are responsible for specific events during cycle division such as microtubule formation and chromatin remodeling. Cyclins can be divided into four classes based on their behavior in the cell cycle of vertebrate somatic cells and yeast cells: G1/S cyclins, S cyclins, M cyclins, G1 cyclins. This division is useful when talking about most cell cycles, but it is not universal as some cyclins have different functions or timing in different cell types.

G1/S Cyclins rise in late G1 and fall in early S phase. The Cdk- G1/S cyclin complex begins to induce the initial processes of DNA replication, primarily by arresting systems that prevent S phase Cdk activity in G1. The cyclins also promote other activities to progress the cell cycle, like centrosome duplication in vertebrates or spindle pole body in yeast. The rise in presence of G1/S cyclins is paralleled by a rise in S cyclins.

S cyclins bind to Cdk and the complex directly induces DNA replication. The levels of S cyclins remain high, not only throughout S phase, but through G2 and early mitosis as well to promote early events in mitosis.

M cyclin concentrations rise as the cell begins to enter mitosis and the concentrations peak at metaphase. Cell changes in the cell cycle like the assembly of mitotic spindles and alignment of sister-chromatids along the spindles are induced by M cyclin- Cdk complexes. The destruction of M cyclins during anaphase causes the exit of mitosis and cytokinesis.

G1 cyclins do not behave like the other cyclins, in that the concentrations increase gradually (with no oscillation), throughout the cell cycle based on cell growth and the external growth-regulatory signals. The presence of G cyclins coordinate cell growth with the entry to a new cell cycle.

Domain structure

Cyclins are generally very different from each other in primary structure, or amino acid sequence. The similarity between members of the cyclin family are similar in the 100 amino acids that make up the cyclin box. Cyclins contain two domains of similar all-Î± fold, the first located at the N-terminus and the second at the C-terminus. All cyclins are believed to contain a similar tertiary structure of two compact domains of 5 Î± helices. The first of which is the conserved cyclin box, outside of which cyclins are divergent. For example, the amino-terminal regions of S and M cyclins contain short destruction-box motifs that target these proteins for proteolysis in mitosis.

Cyclin, N-terminal domain

Structure of bovine cyclin A.[5]

Identifiers	
Symbol	Cyclin_N
Pfam	PF00134
Pfam clan	CL0065
InterPro	IPR006671
PROSITE	PDOC00264
SCOP	1vin

Available PDB structures: [show]

Cyclin, C-terminal domain

Structure of CDK2-cyclin A/indirubin-5-sulphonate.[6]

Identifiers	
Symbol	Cyclin_C
Pfam	PF02984
Pfam clan	CL0065
InterPro	IPR004367
PROSITE	PDOC00264
SCOP	1vin

Available PDB structures: [show]

Types

There are several different cyclins that are active in different parts of the cell cycle and that cause the Cdk to phosphorylate different substrates. There are also several "orphan" cyclins for which no Cdk partner has been identified. For example, cyclin F is an orphan cyclin that is essential for G_2/M transition.[7][8]

Main groups

There are two main groups of cyclins:

- G_1/S cyclins âˆ’ essential for the control of the cell cycle at the G_1/S transition,
  - Cyclin A / CDK2 âˆ’ active in S phase.
  - Cyclin D / CDK4, Cyclin D / CDK6, and Cyclin E / CDK2 âˆ’ regulates transition from G_1 to S phase.
- G_2/M cyclins âˆ’ essential for the control of the cell cycle at the G2/M transition (mitosis). G_2/M cyclins accumulate steadily during G_2 and are abruptly destroyed as cells exit from mitosis (at the end of the M-phase).
  - Cyclin B / CDK1 âˆ’ regulates progression from G_2 to M phase.

Subtypes

Specific cyclin subtypes include:

Species	G1	G1/S	S	M
S. cerevisiae	Cln3 (Cdk1)	Cln 1,2 (Cdk1)	Clb 5,6 (Cdk1)	Clb 1,2,3,4 (Cdk 1)
S. pombe	Puc1? (Cdk1)	Puc1, Cig1? (Cdk1)	Cig2, Cig1? (Cdk1)	Cdc13 (Cdk1)
D. melanogaster	cyclin D (Cdk4)	cyclin E (Cdk2)	cyclin E, A (Cdk2,1)	cyclin A, B, B3 (Cdk1)
X. laevis	either not known or not present	cyclin E (Cdk2)	cyclin E, A (Cdk2,1)	cyclin A, B, B3 (Cdk1)
H. saplens	cyclin D 1,2,3 (Cdk4,6)	cyclin E (Cdk2)	cyclin A (Cdk2,1)	cyclin B (Cdk1)

family	members
A	CCNA1, CCNA2
B	CCNB1, CCNB2, CCNB3
C	CCNC
D	CCND1, CCND2, CCND3
E	CCNE1, CCNE2
F	CCNF
G	CCNG1, CCNG2
H	CCNH
I	CCNI, CCNI2
J	CCNJ, CCNJL
K	CCNK
L	CCNL1, CCNL2
O	CCNO
T	CCNT1, CCNT2
Y	CCNY, CCNYL1, CCNYL2, CCNYL3

Other proteins containing this domain

In addition, the following human proteins contain a cyclin domain:

CABLES2, CNTD1, CNTD2

History

Leland H. Hartwell, R. Timothy Hunt, and Paul M. Nurse won the 2001 Nobel Prize in Physiology or Medicine for their discovery of cyclin and cyclin-dependent kinase.[9]

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Further reading

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v Â· d Â· e **Cell cycle proteins** [show]

Cyclin	A (A1, A2) Â· B (B1, B2, B3) Â· D (D1, D2, D3) Â· E (E1, E2)	
CDK	2 Â· 3 Â· 4 Â· 5 Â· 6 Â· 7 Â· 8 Â· 9 Â· 10 Â· CDK-activating kinase	
CDK inhibitor	p14arf/p16INK4a Â· cip/kip (p21, p27, p57)	
P53 p63 p73 family	p53 Â· p63 Â· p73	
Phases and checkpoints	Interphase	G1 phase Â· S phase Â· G2 phase
	M phase	Mitosis (Preprophase Â· Prophase Â· Prometaphase Â· Metaphase Â· Anaphase Â· Telophase) Â· Cytokinesis

Cell cycle checkpoints	Restriction point Â· Spindle checkpoint Â· Postreplication checkpoint
Other cellular phases	Apoptosis Â· G0 phase Â· Meiosis

B bsyn: dna (repl, cycl, reco, repr) Â· tscr (fact, tcrg, nucl, rnat, rept, ptts) Â· ttln (risu, pttl, nexn) Â· dnab, rnab/rump Â· stru (domn, 1Â°, 2Â°, 3Â°, 4Â°)

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